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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,979	10/22/2003	Stephen Arnold	Poly-46	4703

26479 7590 02/06/2006

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,979	ARNOLD ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 21 November 2005 is acknowledged and has been entered.

Drawings

2. The drawings were received on 21 November 2005. These drawings are acceptable.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-2, 4-5, 10-11, 13-14, 19-22, and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (US 2002/0097401 A1) in view of Boyd et al (US 2004/0023396 A1).

In the instant claims, Maleki et al teach a spherical micro whispering-gallery-mode resonator (i.e. microsphere) coupled to an evanescent coupler (i.e. at least one optical carrier), wherein the resonator has a surface coating that binds to a specific analyte (i.e. receptors), wherein the coupler sends an input beam from a light source to the resonator and carries energy out of the resonator (i.e. applying a light source and detecting light), and wherein changes in mode structure, including the width of the resonance, can be applied to measure analyte binding (i.e. determining a presence of the substance). See page 1, section 0005; page 3, section 0031 ; page 4, sections

0041-0042 ; and page 5, sections 0045-0047. In addition, Maleki et al teach that spherical resonators can support whispering gallery modes, which are electromagnetic field modes confined in an interior region and close to the surface of the sphere around its equator. See page 1, section 0016.

However, Maleki et al fail to teach that the receptors are provided substantially at a belt surface area including an equator of the microsphere, and wherein surface areas of the microsphere other than the belt surface area are substantially free of receptors.

Boyd et al teach one or more probes coupled to a limited region on the surface of a resonator, in order to provide probes in areas where light is confined. See page 3, section 0028. In addition, Boyd et al teach that the resonator is a whispering-gallery-mode resonator. See page 2, section 0018.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of Maleki et al with one or more probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in order to provide probes in areas where light is confined. Since Maleki et al teach that light in a microsphere with whispering gallery modalities are confined to an equatorial region, the probes taught by Boyd et al would be confined to the surface of the microspheres along the equatorial region. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including probes limited to a specific region, as taught by Boyd et al, in the method and apparatus of Maleki et al, since Maleki et al teach capture agents on the surface of a resonator with

whispering gallery mode properties, and the probes of Boyd et al area also immobilized on the surface of a resonator with whispering gallery mode properties.

With regards to claim 2, Maleki et al and Boyd et al references do not explicitly teach an arclength width that is substantially the square root of $R\lambda/2\pi n$. However, the references do teach a microsphere with a band region coupled to an optical fiber, which have a radius R, refractive index n, and wavelength λ. Since the claimed arclength width is dependent upon the limitations of R, n, λ, and a microsphere/optical carrier system, and the microsphere and optical fiber of Maleki et al and Boyd et al teaches the limitations, it would have been obvious to one of ordinary skill in the art at the time of the invention to obtain an arclength width of the square root of $R\lambda/2\pi n$ from the known variables R, n, and λ of a coupled microsphere-fiber optic system.

With regards to claims 4, 13, and 24, Maleki et al teach that microsphere diameters can include 10 microns. See page 1, section 0016.

With regards to claims 20-22, Boyd et al teach that probes include polypeptides and oligonucleotides, and target molecules can include proteins, a viral capsid component, and nucleic acids. See page 3, section 0030 and page 4, section 0034.

7. Claims 3, 6, 12, 15, 23, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (US 2002/0097401 A1) in view of Boyd et al (US 2004/0023396 A1) as applied to claims 1, 10, and 19 above, and further in view of Ganapolskii et al (Measurement Science and Technology, 1997) and Aslam et al (US 4,912,087), and in light of Alexandrov et al (US 3,984,524).

Maleki et al and Boyd et al references have been disclosed above, but fail to teach that the microsphere is formed of amorphous sapphire and that the index of refraction in water is approximately 1.7.

Ganapolskii et al teach a dielectric sphere resonator made from sapphire crystal, in order to provide a measuring resonator with low dielectric losses in the millimeter-wave range. See Abstract.

Aslam et al teach amorphous silicon, in order to provide a highly resistive material. See column 10, lines 34-35.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Maleki et al and Boyd et al with a dielectric sphere resonator made from sapphire crystal, as taught by Ganapolskii et al, in order to provide a measuring resonator with low dielectric losses in the millimeter-wave range, and with amorphous silicon, as taught by Aslam et al, in order to provide a highly resistive material. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a sapphire resonator, wherein the sapphire is amorphous, as taught by Ganapolskii et al and Aslam et al, in the method of Maleki et al and Boyd et al, since Maleki et al and Boyd et al teach microsphere resonators, and the amorphous sapphire sphere of Ganapolskii et al and Aslam et al is one type of material that can act as a resonator.

In addition, although Ganapolskii et al and Aslam et al references do not teach that the index of refraction in water is approximately 1.7, the sapphire sphere taught by

the references inherently has an index of refraction of 1.7 (see Alexandrov et al, column 2, lines 16-17).

8. Claims 7-8 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (US 2002/0097401 A1) in view of Boyd et al (US 2004/0023396 A1) as applied to claims 1 and 10 above, and further in view of Boyd et al (Applied Optics, 2001).

Maleki et al and Boyd et al ('396) references have been disclosed above, but fail to teach that the light source is controlled to emit light in the blue spectrum and at about 400 nm.

Boyd et al (Applied Optics) teach an optical source in the visible range of 400-700 nm, in order to obtain the greatest sensitivity in analysis of biological materials. See page 5743, left column, 2nd paragraph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Maleki et al and Boyd et al ('396) with an optical source in the visible range of 400-700 nm, as taught by Boyd et al (Applied Optics) in order to obtain the greatest sensitivity in analysis of biological materials. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of including an optical source of 400-700 nm, as taught by Boyd et al (Applied Optics), in the method of Maleki et al and Boyd et al ('396), since Maleki et al and Boyd et al ('396) teach an optical source coupled to a resonator that can detect

biological materials, and the optical source of Boyd et al (Applied Optics) is applied for the analysis of biological materials.

9. Claims 9 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maleki et al (US 2002/0097401 A1) in view of Boyd et al (US 2004/0023396 A1) as applied to claims 1 and 10 above, and further in view of Thiele et al (US 5,602,102).

Maleki et al and Boyd et al references have been disclosed above, but fail to teach that a molecule having a mass of about 200,000 Da is captured.

Thiele et al teach dipeptidyl peptidase-I, which has a molecular weight of 200,000 Da, in order to identify an enzyme that is present in high levels of cytotoxic lymphocytes and myeloid cells. See column 1, lines 20-64.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Maleki et al and Boyd et al with dipeptidyl peptidase-I, which has a molecular weight of 200,000 Da, as taught by Thiele et al, in order to identify an enzyme that is present in high levels of cytotoxic lymphocytes and myeloid cells. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including dipeptidyl peptidase-I, as taught by Thiele et al, in the method of Maleki et al and Boyd et al, since Maleki et al and Boyd et al teach the detection of biological molecules, and the dipeptidyl peptidase-I of Thiele et al is one type of biological molecule.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 10/096,333 in view of Boyd et al (US 2004/0023396 A1).

Claims 1-7 of the copending application teach most of the limitations of claims 1-26 of the instant application by disclosing a method for determining the presence or concentration of a substance in a medium, the method comprising providing a sensor in the medium, wherein the sensor includes at least one optical carrier and a microsphere having a surface including receptors for the substrate, each of the at least one optical carrier being coupled with the microsphere, applying a light source to one of the at least

one optical carriers of the sensor, detecting light from one of the at least one optical carriers of the sensor, and determining a presence or concentration of the substance based on a property of the detected light, wherein the property is based on a shift in resonance of the microsphere.

However, claims 1-7 of the copending application fail to teach that the receptors are provided substantially at a belt surface area including an equator of the microsphere, and wherein surface areas of the microsphere other than the belt surface area are substantially free of receptors.

Boyd et al teach one or more probes coupled to a limited region on the surface of a resonator, in order to provide probes in areas where light is confined. See page 3, section 0028. In addition, Boyd et al teach that the resonator is a whispering-gallery-mode resonator. See page 2, section 0018.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of claims 1-7 of the copending application with one or more probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in order to provide probes in areas where light is confined. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in the method of the copending application, since the copending application teach the detection of substances through optical resonance, and the whispering-gallery-mode resonator taught by Boyd et al is one type of material that provides detection of analytes through optical resonance.

This is a provisional obviousness-type double patenting rejection.

12. Claims 1-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/735,247 in view of Boyd et al (US 2004/0023396 A1).

Claims 1-3 of the copending application teach most of the limitations of claims 1-26 of the instant application by disclosing a method for determining the presence or concentration of a substance in a medium, the method comprising providing a sensor in the medium, wherein the sensor includes at least one optical carrier and a microsphere having a surface including receptors for the substrate, each of the at least one optical carrier being coupled with the microsphere, applying a light source to one of the at least one optical carriers of the sensor, detecting a transmission spectra (i.e. light) from one of the at least one optical carriers of the sensor, and determining a presence or concentration of the substance based on a property of the detected light, wherein the property is based on a shift in resonance of the microsphere.

However, claims 1-3 of the copending application fail to teach that the receptors are provided substantially at a belt surface area including an equator of the microsphere, and wherein surface areas of the microsphere other than the belt surface area are substantially free of receptors.

Boyd et al teach one or more probes coupled to a limited region on the surface of a resonator, in order to provide probes in areas where light is confined. See page 3,

section 0028. In addition, Boyd et al teach that the resonator is a whispering-gallery-mode resonator. See page 2, section 0018.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of claims 1-3 of the copending application with one or more probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in order to provide probes in areas where light is confined. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in the method of the copending application, since the copending application teach the detection of substances through an optical change, and the whispering-gallery-mode resonator taught by Boyd et al is one type of material that provides detection of analytes through changes in optical resonance, which is one type of optical change.

This is a provisional obviousness-type double patenting rejection.

13. Claims 1-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34-39 of copending Application No. 10/768,977 in view of Boyd et al (US 2004/0023396 A1).

Claims 1-3 of the copending application teach most of the limitations of claims 1-26 of the instant application by disclosing a method measuring one or more of at least two target substances (i.e. determining the presence of a substance in a medium) using a system including a sensor including at least one optical carrier optically coupled with

both the light source and at least two optical cavities (i.e. each of the at least one optical carrier being coupled with the microsphere), applying a light source to the optical carrier, detecting the resonance excited in the optical cavities a first and second time to determine a change in the characteristic of the resonance of any of the optical cavities (i.e. detecting light from one of the at least one optical carriers of the sensor), and determining a measurement of the target substance using a shift in characteristic of the resonance detected by the detector (i.e. determining a presence of the substance based on a property of detected light, wherein the property is based on a shift in resonance of the microsphere).

However, claims 1-7 of the copending application fail to teach that the receptors are provided substantially at a belt surface area including an equator of the microsphere, and wherein surface areas of the microsphere other than the belt surface area are substantially free of receptors.

Boyd et al teach one or more probes coupled to a limited region on the surface of a resonator, in order to provide probes in areas where light is confined. See page 3, section 0028. In addition, Boyd et al teach that the resonator is a whispering-gallery-mode resonator. See page 2, section 0018.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of claims 34-39 of the copending application with one or more probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in order to provide probes in areas where light is confined. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of

success in including probes coupled to a limited region on the surface of a resonator, as taught by Boyd et al, in the method of the copending application, since the copending application teach the detection of substances through optical resonance, and the whispering-gallery-mode resonator taught by Boyd et al is one type of material that provides detection of analytes through optical resonance.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

14. On page 8 of the response, filed 21 November 2005, Applicants request the withdrawal of the objection to the specification for not describing the reference numbers of Figure 10 since they are described on page 15, lines 3 et seq. The Examiner thanks Applicants for pointing out the proper disclosure of Figure 10 and the objection is hereby withdrawn.

15. Due to the claim amendments, the rejections of claims 2, 11, and 16-17 under 35 U.S.C. 112, 2nd paragraph have been overcome.

16. On pages 10-11, Applicants traverse the rejections applied in the previous Office Action under 35 U.S.C. 103(a) as being obvious over Maleki in view of Boyd. Specifically, Applicants argue that the independent claims 1, 10, and 19 are not rendered obvious by Maleki and Boyd because there is no suggestion to combine these

references. See page 10, 2nd paragraph. Applicants state two reasons as to why one of ordinary skill in the art would not have combined the references:

(1) The Boyd reference merely concerns "including" probes in the region of a ring or disk where light is confined and it is "silent on whether or not the rest of the ring or disk is free of probes. See page 11, 2nd paragraph.

(2) The Boyd sensors are limited to ring and disk resonators and the Boyd reference does not suggest applying its teaching to microsphere resonators.

Applicants' arguments have been fully considered, but are not considered persuasive. With respect to Applicants' first reason above, independent claims 1, 10, and 19 disclose that surface areas of the microsphere other than the belt surface area are ***substantially free of receptors***, which indicates that non-belt surface areas can, but not necessarily, have receptors thereon. Applicants' argument that the Boyd reference merely concerns probes only in a region where light is confined is therefore not persuasive since the claimed language can incorporate the situation where probes are either present or absent on surfaces other than the belt surface area. Nevertheless, Boyd reference provides adequate teaching that teaches the disputed limitation by stating "The ring or disk resonator can also have one or more probes coupled to a surface thereof, ***preferably within the region of the ring or disk where light is confined***". See page 3, section 0028. Since Boyd discloses that the it is ***preferable*** to have probes ***within*** a specific region, it is not preferable to have probes outside of that region, and one of ordinary skill in the art at the time of the invention would recognize

that the best mode of the Boyd resonator is to have the probes confined to light-covered surface areas. The term "preferably" is considered to mean that the probes are intended to be within the light region, but may also be outside of that region. In combining Boyd with Maleki, since Maleki teaches that light is confined to an equator region, the probes would therefore be preferably within the equator region, which is the exact claim language of the independent claims.

With respect to Applicants' second reason above, both Maleki and Boyd references disclose three-dimensional, hollow objects that provide the same manner of analyte detection: whispering-gallery mode. The mere fact that Maleki and Boyd teach different types of structures does not render the references incapable of being combined since the structures perform the same function in the same manner. In addition, it is disclosed in both references that a light region is confined to a specific area of the structure. The rationale, as taught by Boyd, of placing probes preferably within the light region is also capable of being applied to Maleki, since one of ordinary skill in the art at the time of the invention would recognize that only regions exposed to light can propagate a change in resonance due to specific binding involving probes.

Applicants' arguments are therefore not convincing and the rejections made in the previous Office Action have been maintained.

17. On page 11-12 of the response, in the Remarks section, Applicants traverse the rejections of all dependent claims minus 9 and 18 under 35 U.S.C. 103(a) as being obvious over Maleki and Boyd, as described above, and further in view of Ganapolskii,

Alexandrov, and Boyd '2001. Applicants argue that the additional references of Ganapolskii, Alexandrov, and Boyd '2001 do not remedy the deficiencies of Maleki and Boyd. However, as explained above, Maleki and Boyd are proper references applied to the independent claims. Since Applicants have not traversed the instant dependent claims with rationale specific to the dependent claims, Applicants' arguments are not found convincing.

18. On page 13 of the response, in the Remarks section, Applicants traverse the rejection of claims 9 and 18 under 35 U.S.C. 103(a) as being obvious over Maleki and Boyd, as described above, and further in view of Thiele. Specifically, Applicants contend three points:

(1) Applicants argue that the additional Thiele reference does not remedy the deficiencies of Maleki and Boyd.

(2) The Examiner is picking and choosing snippets from various disparate references, which is impermissible hindsight.

(3) Thiele does not meet the limitation that a shift in resonance is detectable where any of the receptors capture ***a single molecule***.

Applicants' arguments have been fully considered, but are not considered to be persuasive. With respect to Applicants' first point above, Maleki and Boyd are proper references applied to the independent claims. Since Applicants have not traversed the

instant dependent claims with rationale specific to the dependent claims, Applicants' arguments are not found convincing.

With respect to Applicants' second point above stating that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). At the time the claimed invention was made, it was well known in the art to detect analytes in same through binding to probes on microspheres (combination of Maleki and Boyd). Since Boyd teaches that proteins can be probes, one of ordinary skill in the art at the time of the invention would have recognized that the combination of Maleki and Boyd references would cover, in general, any analyte type that can bind specifically to proteins. By teaching a specific enzyme that is an indicator for high levels of cytotoxic lymphocytes and myeloid cells, Thiele provides the motivation for wanting to capture such an enzyme. Since enzymes bind to protein substrates, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in applying an enzyme-specific probe on the microsphere to detect the enzyme taught by Thiele.

With respect to Applicants' third point above, it seems as if Applicants are arguing that the instant claims require only one molecule be captured on the entire

microsphere. However, the claims do not support this interpretation. Claims 9 and 18 specifically recite "wherein the shift in resonance of the microsphere is detectable when any of the receptors in the belt surface area capture a single molecule having a mass of about 200,000 Da." The claim is broad enough to encompass Applicants' interpretation and also the situation wherein each receptor binds to a single molecule and that the resonance shift is adjusted for the number of receptors that bind to a molecule. However, Boyd reference actually discloses that the surface can comprise only one receptor, by disclosing that the "resonator can also have one or more probes coupled to a surface thereof". See page 3, section 0028, line 1. In the event that the surface only has one receptor, any binding the occurs on the surface of the microsphere will invariably produce a resonance shift caused by a single molecule, as seemingly interpreted by Applicants.

In light of the arguments above, Applicants' arguments are not found persuasive and the rejections made in the previous Office Action are maintained.

Conclusion

19. No claims are allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum
Patent Examiner
Art Unit 1641

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02/03/06